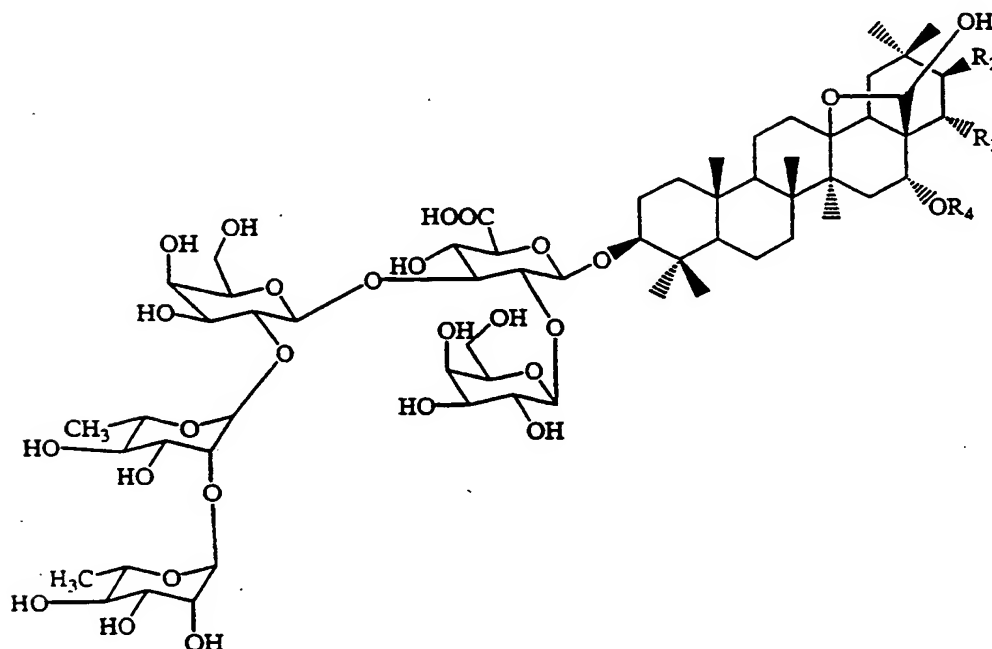


Claims

1. A process for the isolation of triterpene saponins from plants belonging to the family *Myrsinaceae*, characterized in that said process comprises the steps of
  - (a) extracting the dried plant parts with an alcohol and concentrating the extract,
  - 5 (b) removing the apolar fraction from the extract by liquid-liquid extraction with an apolar solvent, and
  - (c) further purifying the saponins in the alcohol extract by liquid -liquid extraction, filtration and chromatography.
- 10 2. A process according to claim 1 wherein the alcohol is methanol, ethanol, isopropanol, butanol, each optionally admixed with water.
3. A process according to claim 1 wherein the saponins of the alcohol extract are further purified by
  - 15 (c6) extracting the aqueous fraction with butanol saturated with water,
  - (c7) evaporating the organic layer to dryness,
  - (c8) washing the residue in a ketone, and
  - (c9) filtering off the crude saponin mixture.
- 20 4. A process according to claim 1 wherein the saponins are isolated from the plant species *Maesa balansae*, and the chromatography comprises straight phase chromatographyliquid chromatography on silicagel or reversed-phase liquid chromatography with gradient eluent system using
  - A : 0.5 % ammonium acetate in water
  - 25 B : methanol
  - C : acetonitrilewherein at  $t = 0$ ,  $(A:B:C) = (60:20:20)$  and  $t = \text{end}$ ,  $(A:B:C) = (0:50:50)$ .
- 30 5. A triterpene saponin obtainable by a process according to anyone of claims 1 to 4.
6. A triterpene saponin according to claim 5 wherein said saponin is isolated from the plant species *Maesa balansae*, and the chromatography comprises reversed-phase liquid chromatography with gradient eluent system using
  - A : 0.5 % ammonium acetate in water
  - 35 B : methanol
  - C : acetonitrilewherein at  $t = 0$ ,  $(A:B:C) = (60:20:20)$  and  $t = \text{end}$ ,  $(A:B:C) = (0:50:50)$ , and wherein said saponin has the following characteristics :

- Compound 1 : MW = 1532,  $\lambda_{\max}$  = 228.6 nm,  $\lambda_{\max 2}$  = 273.3 nm ;  
 Compound 2 : MW = 1510,  $\lambda_{\max}$  = 223.9 nm,  $\lambda_{\max 2}$  = 274.5 nm ;  
 Compound 3 : MW = 1532,  $\lambda_{\max}$  = 279.2 nm,  $\lambda_{\max 2}$  = 223.9 nm ;  
 Compound 4 : MW = 1510,  $\lambda_{\max}$  = 280.4 nm,  $\lambda_{\max 2}$  = 222.7 nm ;  
 5 Compound 5 : MW = 1574,  $\lambda_{\max}$  = 276.8 nm,  $\lambda_{\max 2}$  = 225.0 nm ; or  
 Compound 6 : MW = 1552,  $\lambda_{\max}$  = 279.2 nm,  $\lambda_{\max 2}$  = 223.9 nm.

7. A triterpene saponin having the formula



- 10 wherein  $R_2$  is  $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$  or  $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$ ,  
 $R_3$  is (E) or (Z)  $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$ , and  
 $R_4$  is hydrogen or  $-(\text{C}=\text{O})\text{CH}_3$ .

8. A compound according to claim 7 wherein  
 15 in compound 1,  $R_2$  is  $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$ ,  
 $R_3$  is (Z)  $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$ ,  
 $R_4$  is hydrogen;  
 in compound 2,  $R_2$  is  $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$ ,  
 $R_3$  is (Z)  $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$ ,  
 $R_4$  is hydrogen;  
 20 in compound 3,  $R_2$  is  $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$ ,  
 $R_3$  is (E)  $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$ ,  
 $R_4$  is hydrogen;

in compound 4,  $R_2$  is  $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$ ,  
 $R_3$  is (E)  $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$ ,  
 $R_4$  is hydrogen;

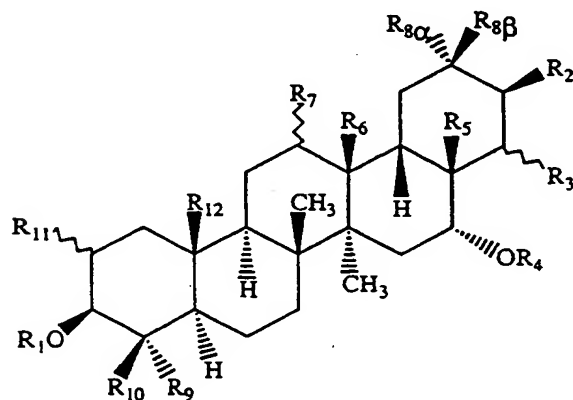
in compound 5,  $R_2$  is  $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$ ,  
 $R_3$  is (E)  $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$ ,  
 $R_4$  is  $-(\text{C}=\text{O})\text{CH}_3$ ;

in compound 6,  $R_2$  is  $-\text{O}(\text{C}=\text{O})\text{C}(\text{CH}_3)=\text{CHCH}_3$ ,  
 $R_3$  is (E)  $-\text{O}(\text{C}=\text{O})\text{CH}=\text{CH}-\text{C}_6\text{H}_5$ ,  
 $R_4$  is  $-(\text{C}=\text{O})\text{CH}_3$ .

9. A pharmaceutical composition comprising a pharmaceutically acceptable excipient and as an active ingredient a triterpene saponin as defined in claim 5, 6, 7 or 8.

10. A composition according to claim 7 adapted for parenteral administration.

11. Use of one or more triterpene saponins for the preparation of a pharmaceutical composition for treating leishmaniasis in hosts infected by *Leishmania* species, characterized in that the saponin has the formula



a stereoisomeric form thereof or a pharmaceutically acceptable addition salt thereof, wherein

$R_1$  is hydrogen,  $-(\text{C}=\text{O})\text{C}_{1.5}\text{alkyl}$ ,  $-(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$ ,  $-(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$  substituted with phenyl, a monosaccharide group or an oligosaccharide group ;

$R_2$  is hydrogen, hydroxy,  $-\text{O}(\text{C}=\text{O})\text{C}_{1.5}\text{alkyl}$ ,  $-\text{O}(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$ ,  $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$ , or  $-\text{O}(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$  substituted with phenyl ;

$R_3$  is hydrogen, hydroxy,  $-\text{O}(\text{C}=\text{O})\text{C}_{1.5}\text{alkyl}$ ,  $-\text{O}(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$ ,  $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$ , or  $-\text{O}(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$  substituted with phenyl ;

$R_4$  is hydrogen,  $\text{C}_{1.6}\text{alkyl}$ ,  $-(\text{C}=\text{O})\text{C}_{1.5}\text{alkyl}$ ,  $-(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$ ,  $-(\text{C}=\text{O})\text{C}_6\text{H}_5$ , or  $-(\text{C}=\text{O})\text{C}_{2.5}\text{alkenyl}$  substituted with phenyl ;

R<sub>5</sub> is CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, CH<sub>2</sub>O-C(=O)CH<sub>3</sub>, CHO, COOH ; or

R<sub>5</sub> and R<sub>2</sub> form a divalent radical of formula -C(=O)-O- ;

R<sub>6</sub> and R<sub>7</sub> are hydrogen; or taken together they form a bond; or

R<sub>5</sub> and R<sub>6</sub> form a divalent radical of formula

5        -CH<sub>2</sub>-O-                (a),

         -CH(OR<sub>13</sub>)-O-        (b),

         -C(=O)-O-            (c),

         wherein R<sub>13</sub> is hydrogen, C<sub>1-6</sub>alkyl or -(C=O)C<sub>1-5</sub>alkyl ;

R<sub>8α</sub> and R<sub>8β</sub> each independently represent CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>,

10       CH<sub>2</sub>O-C(=O) C<sub>1-5</sub>alkyl, CHO, CH(OCH<sub>3</sub>)<sub>2</sub>, CH=NOH, COOH ;

         R<sub>8β</sub> and R<sub>3</sub> form a divalent radical of formula -C(=O)-O- ;

R<sub>8β</sub> and R<sub>5</sub> form a divalent radical of formula -CH<sub>2</sub>O-CHOH- ;

R<sub>9</sub> is CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, CH<sub>2</sub>O-C(=O)C<sub>1-5</sub>alkyl, CHO, COOH ;

R<sub>10</sub> is CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, CH<sub>2</sub>O-C(=O)C<sub>1-5</sub>alkyl, CHO, COOH ;

15       R<sub>11</sub> is hydrogen, hydroxy or O-C(=O)C<sub>1-5</sub>alkyl ; or R<sub>10</sub> and R<sub>11</sub> form a divalent  
         radical of formula -CH<sub>2</sub>O- ; and

R<sub>12</sub> is CH<sub>3</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, CH<sub>2</sub>O-C(=O)CH<sub>3</sub>, CHO, CH=NOH, or COOH.

12. Use according to claim 11 wherein

20       R<sub>1</sub> is hydrogen, -(C=O)C<sub>1-5</sub>alkyl, or an oligosaccharide group ;

R<sub>3</sub> is hydrogen, hydroxy, -O(C=O)C<sub>1-5</sub>alkyl, -O(C=O)C<sub>2-5</sub>alkenyl,  
         -O(C=O)C<sub>2-5</sub>alkenyl substituted with phenyl ;

R<sub>4</sub> is hydrogen, C<sub>1-6</sub>alkyl, -(C=O)C<sub>1-5</sub>alkyl, -(C=O)C<sub>2-5</sub>alkenyl ;

R<sub>5</sub> is CH<sub>2</sub>OH, CH<sub>2</sub>O-C(=O)CH<sub>3</sub>, CHO ; and

25       R<sub>6</sub> and R<sub>7</sub> taken together form a bond; or

R<sub>5</sub> and R<sub>6</sub> form a divalent radical of formula

         -CH<sub>2</sub>-O-                (a),

         -CH(OR<sub>13</sub>)-O-        (b),

         -C(=O)-O-            (c),

30       wherein R<sub>13</sub> is hydrogen, C<sub>1-6</sub>alkyl or -(C=O)C<sub>1-5</sub>alkyl, ; and

R<sub>7</sub> is hydrogen ;

R<sub>8β</sub> represents CH<sub>3</sub>, CH<sub>2</sub>OH, CHO, CH(OCH<sub>3</sub>)<sub>2</sub>, CH=NOH, COOH ;

R<sub>8α</sub> represents CH<sub>3</sub> ;

R<sub>8β</sub> and R<sub>3</sub> form a divalent radical of formula -C(=O)-O- ; or

35       R<sub>8β</sub> and R<sub>5</sub> form a divalent radical of formula -CH<sub>2</sub>O-CHOH- ;

R<sub>10</sub> is CH<sub>3</sub>, CH<sub>2</sub>OH ;

R<sub>11</sub> is hydrogen, hydroxy or O-C(=O)C<sub>1-5</sub>alkyl ; or

$R_{10}$  and  $R_{11}$  form a divalent radical of formula  $-\text{CH}_2\text{O}-$  ; and  
 $R_{12}$  is  $\text{CH}_3$ ,  $\text{CH}_2\text{OH}$ ,  $\text{CH}_2\text{O}-\text{C}(=\text{O})\text{CH}_3$ ,  $\text{CHO}$ , or  $\text{CH}=\text{NOH}$ .

13. Use according to claim 12 wherein

5  $R_1$  is hydrogen or an oligosaccharide group ;

$R_2$  is hydrogen, hydroxy,  $-\text{O}(\text{C}=\text{O})\text{C}_{1-5}\text{alkyl}$ ,  $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$ ,  $-\text{O}(\text{C}=\text{O})\text{C}_6\text{H}_5$ ,  
 or  $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$  substituted with phenyl ;

$R_3$  is hydrogen, hydroxy,  $-\text{O}(\text{C}=\text{O})\text{C}_{1-5}\text{alkyl}$ ,  $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$ ,  
 $-\text{O}(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$  substituted with phenyl ;

10  $R_4$  is hydrogen,  $\text{C}_{1-6}\text{alkyl}$ ,  $-(\text{C}=\text{O})\text{C}_{1-5}\text{alkyl}$ ,  $-(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$ ,  $-(\text{C}=\text{O})\text{C}_{2-5}\text{alkenyl}$   
 substituted with phenyl ;

$R_5$  is  $\text{CH}_2\text{OH}$ ,  $\text{CH}_2\text{OCH}_3$ ,  $\text{CH}_2\text{O}-\text{C}(=\text{O})\text{CH}_3$ ,  $\text{CHO}$ ,  $\text{COOH}$  ; and

$R_6$  and  $R_7$  taken together form a bond; or

$R_5$  and  $R_6$  form a divalent radical of formula

15  $-\text{CH}_2-\text{O}-$  (a),

$-\text{CH}(\text{OR}_{13})-\text{O}-$  (b),

$-\text{C}(=\text{O})-\text{O}-$  (c),

wherein  $R_{13}$  is hydrogen ; and

$R_7$  is hydrogen ;

20  $R_{8\alpha}$  and  $R_{8\beta}$  both represent  $\text{CH}_3$  ;

$R_9$  is  $\text{CH}_3$  ;

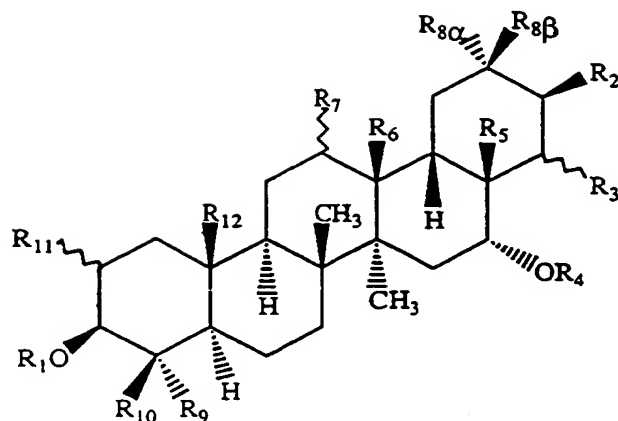
$R_{10}$  is  $\text{CH}_3$  ;

$R_{11}$  is hydrogen ; and

$R_{12}$  is  $\text{CH}_3$ .

25

14. A method of alleviating clinical manifestations of, and curing disorders known as leishmaniasis attributable to infection by protozoan parasites of the genus *Leishmania* in both men and animals, comprising administering to an infected host a therapeutically effective amount of a compound of formula:



a stereoisomeric form thereof or a pharmaceutically acceptable addition salt thereof, wherein

$R_1$  is hydrogen,  $-(C=O)C_{1-5}alkyl$ ,  $-(C=O)C_{2-5}alkenyl$ ,  $-(C=O)C_{2-5}alkenyl$  substituted with phenyl, a monosaccharide group or an oligosaccharide group ;

$R_2$  is hydrogen, hydroxy,  $-O(C=O)C_{1-5}alkyl$ ,  $-O(C=O)C_{2-5}alkenyl$ ,  $-O(C=O)C_6H_5$ , or  $-O(C=O)C_{2-5}alkenyl$  substituted with phenyl ;

$R_3$  is hydrogen, hydroxy,  $-O(C=O)C_{1-5}alkyl$ ,  $-O(C=O)C_{2-5}alkenyl$ ,  $-O(C=O)C_6H_5$ , or  $-O(C=O)C_{2-5}alkenyl$  substituted with phenyl ;

$R_4$  is hydrogen,  $C_{1-6}alkyl$ ,  $-(C=O)C_{1-5}alkyl$ ,  $-(C=O)C_{2-5}alkenyl$ ,  $-(C=O)C_6H_5$ , or  $-(C=O)C_{2-5}alkenyl$  substituted with phenyl ;

$R_5$  is  $CH_3$ ,  $CH_2OH$ ,  $CH_2OCH_3$ ,  $CH_2O-C(=O)CH_3$ ,  $CHO$ ,  $COOH$  ; or

$R_5$  and  $R_2$  form a divalent radical of formula  $-C(=O)-O-$  ;

$R_6$  and  $R_7$  are hydrogen; or taken together they form a bond; or

$R_5$  and  $R_6$  form a divalent radical of formula

$-CH_2-O-$  (a),

$-CH(OR_{13})-O-$  (b),

$-C(=O)-O-$  (c),

wherein  $R_{13}$  is hydrogen,  $C_{1-6}alkyl$  or  $-(C=O)C_{1-5}alkyl$  ;

$R_{8\alpha}$  and  $R_{8\beta}$  each independently represent  $CH_3$ ,  $CH_2OH$ ,  $CH_2OCH_3$ ,  $CH_2O-C(=O)C_{1-5}alkyl$ ,  $CHO$ ,  $CH(OCH_3)_2$ ,  $CH=NOH$ ,  $COOH$  ;

$R_{8\beta}$  and  $R_3$  form a divalent radical of formula  $-C(=O)-O-$  ;

$R_{8\beta}$  and  $R_5$  form a divalent radical of formula  $-CH_2O-CHOH-$  ;

$R_9$  is  $CH_3$ ,  $CH_2OH$ ,  $CH_2OCH_3$ ,  $CH_2O-C(=O)C_{1-5}alkyl$ ,  $CHO$ ,  $COOH$  ;

$R_{10}$  is  $CH_3$ ,  $CH_2OH$ ,  $CH_2OCH_3$ ,  $CH_2O-C(=O)C_{1-5}alkyl$ ,  $CHO$ ,  $COOH$  ;

$R_{11}$  is hydrogen, hydroxy or  $O-C(=O)C_{1-5}alkyl$  ; or  $R_{10}$  and  $R_{11}$  form a divalent radical of formula  $-CH_2O-$  ; and

$R_{12}$  is  $CH_3$ ,  $CH_2OH$ ,  $CH_2OCH_3$ ,  $CH_2O-C(=O)CH_3$ ,  $CHO$ ,  $CH=NOH$ , or  $COOH$ .